Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

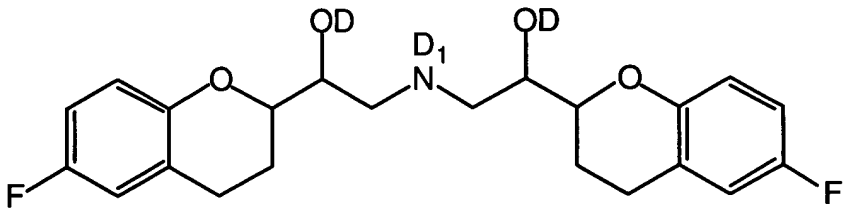
Listing of Claims:

1. (Currently Amended) Nebivolol and/or a metabolite of nebivolol, or a stereoisomer thereof, having at least one NO group, at least one NO_2 group, or at least one NO and NO_2 group, or a pharmaceutically acceptable salt thereof, wherein the at least one NO group, at least one NO_2 group, or the at least one NO and NO_2 group is linked to the nebivolol and/or metabolite of nebivolol through an oxygen atom, a nitrogen atom or a sulfur atom.

2. (Currently Amended) Nebivolol and/or a metabolite of nebivolol, or a stereoisomer thereof, having at least one NO group or at least one NO and NO_2 group, or a pharmaceutically acceptable salt thereof, wherein the at least one NO group or at least one NO and NO_2 group is linked to the nebivolol and/or metabolite of nebivolol through an oxygen atom, a nitrogen atom or a sulfur atom.

3. (Currently Amended) A compound of Formula (I), ~~Formula (II), Formula (III),~~ Formula (IV) or Formula (V), an isomer thereof or a pharmaceutically acceptable salt thereof:

wherein the compound of Formula (I) is:

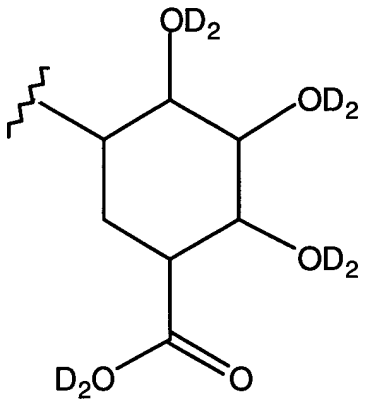


I

wherein:

D is hydrogen, Q, K or R_5;

R_5 is:



D_1 is hydrogen or R_5;

D_2 is hydrogen, Q or K;

Q is –NO or $-NO_2$;

K is $-W_a-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-$ T-Q;

a, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently -C(O)-, -C(S)-, -T-, $-(C(R_e)(R_f))_h-$, an alkyl group, an aryl group, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

E at each occurrence is independently -T-, an alkyl group, an aryl group, $-(C(R_e)(R_f))_h-$, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

h is an integer form 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, an alkylcycloalkyl, an alkylheterocyclic ring, a cycloalkylalkyl, a cycloalkylthio, a cycloalkenyl, an heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an

alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, arylsulphonyloxy, a sulfonic ester, a urea, a phosphoryl, a nitro, W_h, -T-Q , or $-(C(R_e)(R_f))_k$-T-Q, or R_e and R_f taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group, an aryl group, an oxime or a bridged cycloalkyl group;

k is an integer from 1 to 3;

T at each occurrence is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o-$ or $-N(R_a)R_i-$;

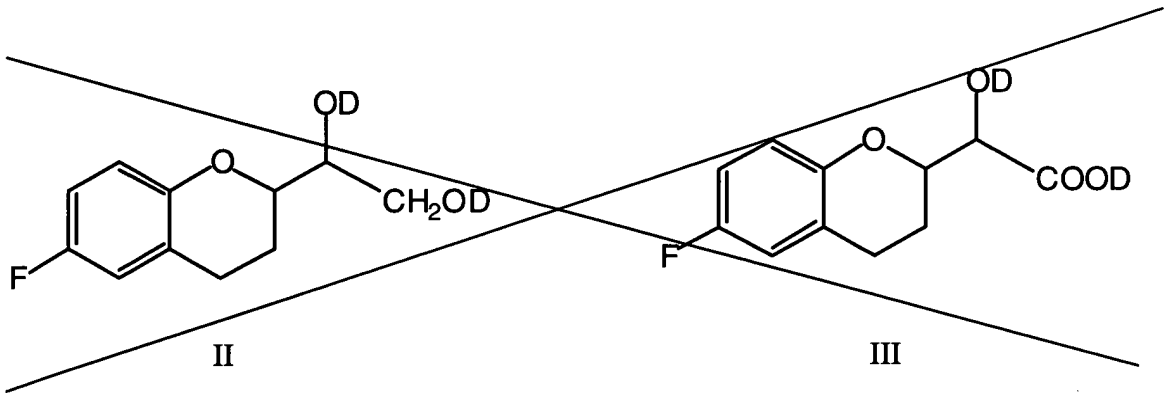
o is an integer from 0 to 2;

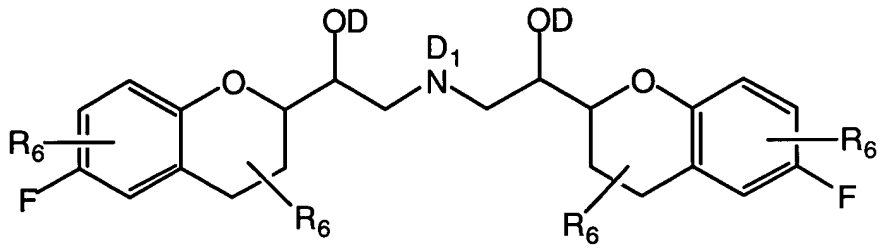
R_a is a lone pair of electrons, a hydrogen or an alkyl group;

R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyl, arylsulphonyloxy, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-CH_2-C(T-Q)(R_e)(R_f)$, a bond to an adjacent atom creating a double bond to that atom, $-(N_2O_2-)^-\bullet M^+$, wherein M^+ is an organic or inorganic cation;

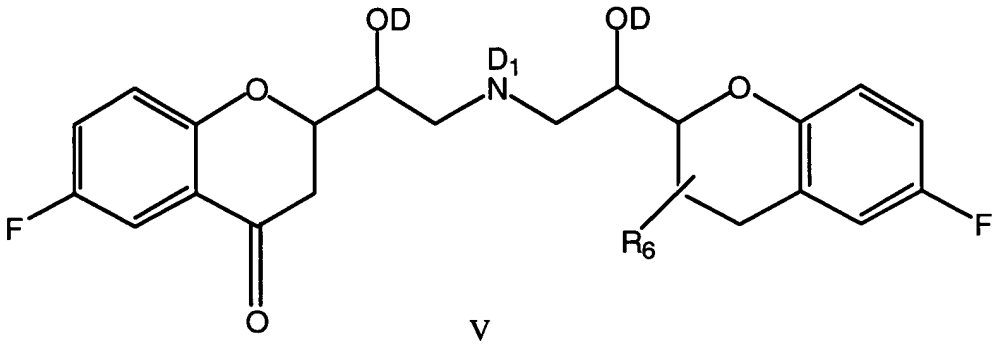
with the proviso that the compound of Formula (I) must contain at least one nitrite, nitrate, thionitrite or thionitrate group;

wherein the compounds of ~~Formula (II), Formula (III),~~ Formula (IV) and Formula (V) are:





IV



V

wherein:

R_6 at each occurrence is independently a hydrogen, a hydroxy or -OD;

D and D_1 are as defined herein; and

with the proviso that the compounds of ~~Formula (II), Formula (III),~~ Formula (IV) and Formula (V), must contain at least one nitrite, nitrate, thionitrite or thionitrate group.

4. (Currently Amended) The compound of claim 3, wherein the compound of Formula (I) is a nitrosated nebivolol, a nitrosylated nebivolol, or a nitrosated and nitrosylated nebivolol, wherein the compounds of ~~Formula (II), Formula (III),~~ Formula (IV) and Formula (V) are a nitrosated metabolite of nebivolol, a nitrosylated metabolite of nebivolol, or a nitrosated and nitrosylated metabolite of nebivolol.

5. (Original) A composition comprising the compound of claim 3 and a pharmaceutically acceptable carrier.

6. (Currently Amended) A method of treating ~~and/or preventing~~ a vascular disease ~~characterized by~~ due to nitric oxide insufficiency in a patient in need thereof comprising administering a therapeutically effective amount of the composition of claim 5.

7. (Currently Amended) The method of claim 6, wherein the vascular disease ~~characterized by~~ due to nitric oxide insufficiency is a cardiovascular disease; a disease resulting from oxidative stress; low-renin hypertension; salt-sensitive hypertension; low-renin, salt-sensitive hypertension; primary pulmonary hypertension; thromboembolic pulmonary hypertension; pregnancy-induced hypertension; renovascular hypertension; hypertension-dependent end-stage renal disease; heart failure; microvascular cardiac ischemia; left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction.

8. (Original) The method of claim 7, wherein the cardiovascular disease is congestive heart failure, hypertension, pulmonary hypertension, myocardial and cerebral infarctions, atherosclerosis, atherogenesis, thrombosis, ischemic heart disease, post-angioplasty restenosis, coronary artery diseases, renal failure, stable, unstable and variant (Prinzmetal) angina, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, transient ischemic attacks, cerebrovascular accidents, restenosis, controlling blood pressure in hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, pulmonary edema, vascular complications associated with the use of medical devices, wounds associated with the use of medical devices, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or bleeding disorders.

9. (Original) The method of claim 8, wherein the cardiovascular disease is congestive heart failure, hypertension, restenosis or atherosclerosis.

10. (Original) The method of claim 7, wherein the disease resulting from oxidative stress is atherogenesis, atheromatosis, arteriosclerosis, artherosclerosis, vascular hypertrophy associated with hypertension, hyperlipoproteinaemia, normal vascular degeneration through aging, parathyroidal reactive hyperplasia, chronic renal disease, a neoplastic disease, an inflammatory disease, a neurological and acute bronchopulmonary disease, a tumorigenesis, an ischemia-reperfusion syndrome, arthritis or sepsis.

11. (Original) The method of claim 6, wherein the composition is administered intravenously, orally, bucally, parenterally, by an inhalation spray, by topical application or transdermally.

12. (Original) A method of treating Raynaud's syndrome in a patient comprising administering to the patient a therapeutically effective amount of the composition of claim 5.

13. (Original) The method of claim 12, wherein the composition is administered orally or transdermally.

14. (Original) The method of claim 13, wherein the transdermal application is a sustained-release patch.

15. (Original) A composition comprising at least one compound of claim 3, or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, and at least one compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase or a pharmaceutically acceptable salt thereof.

16. (Original) The composition of claim 15, wherein the at least one compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.

17. (Original) The composition of claim 16, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione or S-nitroso-cysteinyl-glycine.

18. (Original) The composition of claim 16, wherein the S-nitrosothiol is:

(i) $HS(C(R_e)(R_f))_mSNO$;

(ii) $ONS(C(R_e)(R_f))_mR_e$; and

(iii) $H_2N\text{-}CH(CO_2H)\text{-}(CH_2)_m\text{-}C(O)NH\text{-}CH(CH_2SNO)\text{-}C(O)NH\text{-}CH_2\text{-}CO_2H$;

wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, an alkylcycloalkyl, an alkylheterocyclic ring, a cycloalkylalkyl, a cycloalkylthio, a cycloalkenyl, an heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an

ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, arylsulphonyloxy, a sulfonic ester, a urea, a phosphoryl, a nitro, W_h, -T-Q , or -$(C(R_e)(R_f))_k$-T-Q, or R_e and R_f taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group, an aryl group, an oxime or a bridged cycloalkyl group; Q is -NO or -NO_2; and T is independently a covalent bond, a carbonyl, an oxygen, -$S(O)_o$- or -$N(R_a)R_i$-; wherein o is an integer from 0 to 2; R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyl, arylsulphonyloxy, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, -CH_2-$C(T-Q)(R_e)(R_f)$, a bond to an adjacent atom creating a double bond to that atom, -$(N_2O_2-)^-$•M^+, wherein M^+ is an organic or inorganic cation; with the proviso that when R_i is -CH_2-$C(T-Q)(R_e)(R_f)$ or -(N_2O_2-)•M^+; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group.

19. (Original) The composition of claim 15, wherein the at least one compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:

(i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;

(ii) a compound that comprises at least one O_2N-O-, O_2N-N-, O_2N-S- or -O_2N-C- group;

(iii) a N-oxo-N-nitrosoamine having the formula: R^1R^2N-N(O-M^+)-NO, wherein R^1 and R^2 are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M^+ is an organic or inorganic cation.

20. (Original) The composition of claim 19, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-O-polypeptide, an ON-N-polypepetide, an ON-C-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-C-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-C-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted,

aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-C-hydrocarbon, an ON-O-heterocyclic compound, an ON-N-heterocyclic compound or a ON-C-heterocyclic compound.

21. (Original) The composition of claim 19, wherein compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group is an O_2N-O-polypeptide, an O_2N-N-polypeptide, an O_2N-S-polypeptide, an O_2N-C-polypeptide, an O_2N-O-amino acid, O_2N-N-amino acid, O_2N-S-amino acid, an O_2N-C-amino acid, an O_2N-O-sugar, an O_2N-N-sugar, O_2N-S-sugar, an O_2N-C-sugar, an O_2N-O-oligonucleotide, an O_2N-N-oligonucleotide, an O_2N-S-oligonucleotide, an O_2N-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-S-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O_2N-C-hydrocarbon, an O_2N-O-heterocyclic compound, an O_2N-N-heterocyclic compound, an O_2N-S-heterocyclic compound or an O_2N-C-heterocyclic compound.

22. (Original) The composition of claim 21, wherein compound comprising at least one O_2N-O-, O_2N-N-, O_2N-S- or O_2N-C- group is isosorbide mononitrate and/or isosorbide dinitrate.

23. (Original) The composition of claim 15, wherein the at least one compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine, lysine, polypeptides comprising at least one of these amino acids or inhibitors of the enzyme arginase.

24. (Currently Amended) A method of treating ~~and/or preventing~~ a vascular disease ~~characterized by~~ due to nitric oxide insufficiency in a patient in need thereof comprising administering a therapeutically effective amount of the composition of claim 15.

25. (Currently Amended) The method of claim 24, wherein the vascular disease ~~characterized by~~ due to nitric oxide insufficiency is a cardiovascular disease; a disease resulting

from oxidative stress; low-renin hypertension; salt-sensitive hypertension; low-renin, salt-sensitive hypertension; primary pulmonary hypertension; thromboembolic pulmonary hypertension; pregnancy-induced hypertension; renovascular hypertension; hypertension-dependent end-stage renal disease; heart failure; microvascular cardiac ischemia; left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction.

26. (Original) The method of claim 25, wherein the cardiovascular disease is congestive heart failure, hypertension, pulmonary hypertension, myocardial and cerebral infarctions, atherosclerosis, atherogenesis, thrombosis, ischemic heart disease, post-angioplasty restenosis, coronary artery diseases, renal failure, stable, unstable and variant (Prinzmetal) angina, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, transient ischemic attacks, cerebrovascular accidents, restenosis, controlling blood pressure in hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, pulmonary edema, vascular complications associated with the use of medical devices, wounds associated with the use of medical devices, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or bleeding disorders.

27. (Original) The method of claim 26, wherein the cardiovascular disease is congestive heart failure, hypertension, restenosis or atherosclerosis.

28. (Original) The method of claim 25, wherein the disease resulting from oxidative stress is atherogenesis, atheromatosis, arteriosclerosis, artherosclerosis, vascular hypertrophy associated with hypertension, hyperlipoproteinaemia, normal vascular degeneration through aging, parathyroidal reactive hyperplasia, chronic renal disease, a neoplastic disease, an inflammatory disease, a neurological and acute bronchopulmonary disease, a tumorigenesis, an ischemia-reperfusion syndrome, arthritis or sepsis.

29. (Original) The method of claim 24, wherein the composition is administered intravenously, orally, bucally, parenterally, by an inhalation spray, by topical application or transdermally.

30. (Original) A method of treating Raynaud's syndrome in a patient comprising administering to the patient a therapeutically effective amount of the composition of claim 15.

31. (Original) The method of claim 30, wherein the composition is administered orally or transdermally.

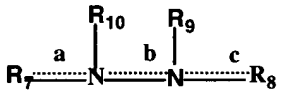
32. (Original) The method of claim 31, wherein the transdermal application is a sustained-release patch.

33. (Currently Amended) The composition of claim 3, further comprising at least one antioxidant, wherein the antioxidant is a small-molecule antioxidant, or a pharmaceutically acceptable salt thereof, or an antioxidant enzyme.

34. (Cancelled)

35. (Currently Amended) The composition of claim ~~34~~ 33, wherein the small-molecule antioxidant is a hydralazine compound of Formula (VI), a glutathione, a vitamin C, a vitamin E, a cysteine, a N-acetyl-cysteine, a β-carotene, an ubiquinone, an ubiquinol-10, a tocopherol, a coenzyme Q, or a mixture thereof;

wherein the hydralazine compound of Formula (VI) is:



(VI)

wherein a, b and c are independently a single or double bond; R_7 and R_8 are each independently a hydrogen, an alkyl, an ester or a heterocyclic ring; R_9 and R_{10} are each independently a lone pair of electrons or a hydrogen; with the proviso that at least one of R_7, R_8, R_9 and R_{10} is not a hydrogen.

36. (Currently Amended) The composition of claim ~~34~~ 33, wherein the antioxidant enzyme is a superoxide dismutase, a catalase, a glutathione peroxidase, or a mixture thereof.

37. (Original) The composition of claim 35, wherein the hydralazine compound is budralazine, cadralazine, dihydralazine, endralazine, hydralazine, pildralazine or todralazine or a pharmaceutically acceptable salt thereof.

38. (Original) The composition of claim 37, wherein the hydralazine compound is hydralazine hydrochloride.

39. (Currently Amended) A method of treating ~~and/or preventing~~ a vascular disease ~~characterized by~~ due to nitric oxide insufficiency in a patient in need thereof comprising administering a therapeutically effective amount of the composition of claim 33.

40. (Currently Amended) The method of claim 39, wherein the vascular disease ~~characterized by~~ due to nitric oxide insufficiency is a cardiovascular disease; a disease resulting

from oxidative stress; low-renin hypertension; salt-sensitive hypertension; low-renin, salt-sensitive hypertension; primary pulmonary hypertension; thromboembolic pulmonary hypertension; pregnancy-induced hypertension; renovascular hypertension; hypertension-dependent end-stage renal disease; heart failure; microvascular cardiac ischemia; left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction.

41. (Original) The method of claim 40, wherein the cardiovascular disease is congestive heart failure, hypertension, pulmonary hypertension, myocardial and cerebral infarctions, atherosclerosis, atherogenesis, thrombosis, ischemic heart disease, post-angioplasty restenosis, coronary artery diseases, renal failure, stable, unstable and variant (Prinzmetal) angina, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, transient ischemic attacks, cerebrovascular accidents, restenosis, controlling blood pressure in hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, pulmonary edema, vascular complications associated with the use of medical devices, wounds associated with the use of medical devices, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or bleeding disorders.

42. (Original) The method of claim 41, wherein the cardiovascular disease is congestive heart failure, hypertension, restenosis or atherosclerosis.

43. (Original) The method of claim 40, wherein the disease resulting from oxidative stress is atherogenesis, atheromatosis, arteriosclerosis, artherosclerosis, vascular hypertrophy associated with hypertension, hyperlipoproteinaemia, normal vascular degeneration through aging, parathyroidal reactive hyperplasia, chronic renal disease, a neoplastic disease, an inflammatory disease, a neurological and acute bronchopulmonary disease, a tumorigenesis, an ischemia-reperfusion syndrome, arthritis or sepsis.

44. (Original) The method of claim 39, wherein the composition is administered intravenously, orally, bucally, parenterally, by an inhalation spray, by topical application or transdermally.

45. (Original) A method of treating Raynaud's syndrome in a patient comprising administering to the patient a therapeutically effective amount of the composition of claim 33.

46. (Original) The method of claim 45, wherein the composition is administered orally or transdermally.

47. (Original) The method of claim 46, wherein the transdermal application is a sustained-release patch.

48. (Currently Amended) The composition of claim 3, further comprising at least one nitrosated compound used to treat cardiovascular diseases, wherein the nitrosated compound used to treat cardiovascular diseases is a nitrosated angiotensin-converting enzyme inhibitor, a nitrosated beta-adrenergic blocker, a nitrosated cholesterol reducer, a nitrosated calcium channel blocker, a nitrosated endothelin antagonist, a nitrosated angiotensin II receptor antagonist, or a nitrosated renin inhibitor.

49. (Cancelled)

50. (Currently Amended) A method of treating ~~and/or preventing~~ a vascular disease ~~characterized by~~ due to nitric oxide insufficiency in a patient in need thereof comprising administering a therapeutically effective amount of the composition of claim 48.

51. (Currently Amended) The method of claim 50, wherein the vascular disease ~~characterized by~~ due to nitric oxide insufficiency is a cardiovascular disease; a disease resulting from oxidative stress; low-renin hypertension; salt-sensitive hypertension; low-renin, salt-sensitive hypertension; primary pulmonary hypertension; thromboembolic pulmonary hypertension; pregnancy-induced hypertension; renovascular hypertension; hypertension-dependent end-stage renal disease; heart failure; microvascular cardiac ischemia; left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction.

52. (Original) The method of claim 51, wherein the cardiovascular disease is congestive heart failure, hypertension, pulmonary hypertension, myocardial and cerebral infarctions, atherosclerosis, atherogenesis, thrombosis, ischemic heart disease, post-angioplasty restenosis, coronary artery diseases, renal failure, stable, unstable and variant (Prinzmetal) angina, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, transient ischemic attacks, cerebrovascular accidents, restenosis, controlling blood pressure in hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, pulmonary edema, vascular complications associated with the use of medical devices, wounds associated with the use of medical devices, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or bleeding disorders.

53. (Original) The method of claim 52, wherein the cardiovascular disease is congestive heart failure, hypertension, restenosis or atherosclerosis.

54. (Original) The method of claim 51, wherein the disease resulting from oxidative stress is atherogenesis, atheromatosis, arteriosclerosis, artherosclerosis, vascular hypertrophy associated with hypertension, hyperlipoproteinaemia, normal vascular degeneration through aging, parathyroidal reactive hyperplasia, chronic renal disease, a neoplastic disease, an inflammatory disease, a neurological and acute bronchopulmonary disease, a tumorigenesis, an ischemia-reperfusion syndrome, arthritis or sepsis.

55. (Original) The method of claim 50, wherein the composition is administered intravenously, orally, bucally, parenterally, by an inhalation spray, by topical application or transdermally.

56. (Original) A method of treating Raynaud's syndrome in a patient comprising administering to the patient a therapeutically effective amount of the composition of claim 48.

57. (Original) The method of claim 56, wherein the composition is administered orally or transdermally.

58. (Original) The method of claim 57, wherein the transdermal application is a sustained-release patch.

59. (Currently Amended) The composition of claim 3, further comprising at least ~~one compound used to treat cardiovascular diseases~~, one angiotensin-converting enzyme inhibitor, beta-adrenergic blocker, cholesterol reducer, calcium channel blocker, angiotensin II receptor antagonist, endothelin antagonist, renin inhibitor, or a pharmaceutically acceptable salt thereof.

60. (Cancelled)

61. (Currently Amended) A method of treating ~~and/or preventing~~ a vascular disease ~~characterized by~~ due to nitric oxide insufficiency in a patient in need thereof comprising administering a therapeutically effective amount of the composition of claim 59.

62. (Currently Amended) The method of claim 61, wherein the vascular disease ~~characterized by~~ due to nitric oxide insufficiency is a cardiovascular disease; a disease resulting from oxidative stress; low-renin hypertension; salt-sensitive hypertension; low-renin, salt-sensitive hypertension; primary pulmonary hypertension; thromboembolic pulmonary hypertension; pregnancy-induced hypertension; renovascular hypertension; hypertension-dependent end-stage renal disease; heart failure; microvascular cardiac ischemia; left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction.

63. (Original) The method of claim 62, wherein the cardiovascular disease is congestive heart failure, hypertension, pulmonary hypertension, myocardial and cerebral infarctions, atherosclerosis, atherogenesis, thrombosis, ischemic heart disease, post-angioplasty restenosis, coronary artery diseases, renal failure, stable, unstable and variant (Prinzmetal) angina, cardiac edema, renal insufficiency, nephrotic edema, hepatic edema, stroke, transient ischemic attacks, cerebrovascular accidents, restenosis, controlling blood pressure in hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, pulmonary edema, vascular complications associated with the use of medical devices, wounds associated with the use of medical devices, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or bleeding disorders.

64. (Original) The method of claim 63, wherein the cardiovascular disease or disorder is congestive heart failure, hypertension, restenosis or atherosclerosis.

65. (Original) The method of claim 62, wherein the disease resulting from oxidative stress is atherogenesis, atheromatosis, arteriosclerosis, artherosclerosis, vascular hypertrophy associated with hypertension, hyperlipoproteinaemia, normal vascular degeneration through aging, parathyroidal reactive hyperplasia, chronic renal disease, a neoplastic disease, an inflammatory disease, a neurological and acute bronchopulmonary disease, a tumorigenesis, an ischemia-reperfusion syndrome, arthritis or sepsis.

66. (Original) The method of claim 61, wherein the composition is administered intravenously, orally, bucally, parenterally, by an inhalation spray, by topical application or transdermally.

67. (Original) The method of claim 61, further comprising administering a digitalis.

68. (Original) The method of claim 67, wherein the digitalis is digoxin

69. (Original) The method of claim 67, wherein the digoxin is administered in an amount to achieve a blood serum concentration of at least about 0.7 nanograms per milliliter to about 2.0 nanograms per milliliter.

70. (Currently Amended) The method of claim 61 further comprising administering a therapeutically effective edema managing amount of a diuretic compound, wherein the diuretic compound is a thiazide, ethacrynic acid, a furosemide, a spiranolactone, a triamterene, or a mixture thereof.

71. (Cancelled)

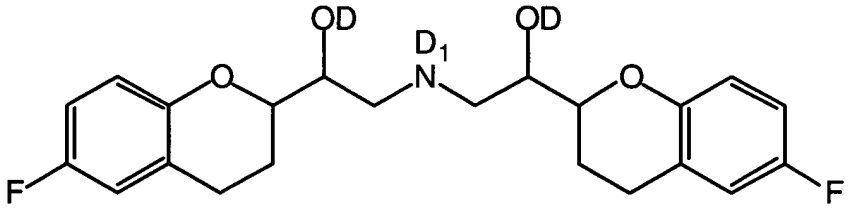
72. (Original) The method of claim 70, further comprising administering a therapeutically effective amount of potassium.

73. (Original) The method of claim 72, wherein the potassium is administered as potassium chloride or by the daily ingestion of foods with high potassium content.

74. (Currently Amended) A composition comprising at least one compound of Formula (I), ~~Formula (II), Formula (III),~~ Formula (IV) or Formula (V), or an isomer thereof, or a pharmaceutically acceptable salt thereof, bound to a matrix;

wherein the matrix is a polymer, a fiber, or a mixture thereof; and

wherein the compound of Formula (I) is:

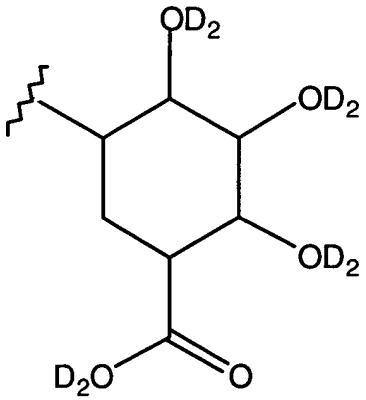


I

wherein:

D is hydrogen, Q, K or R_5;

R_5 is:



D_1 is hydrogen or R_5;

D_2 is hydrogen, Q or K;

Q is –NO or $-NO_2$;

K is $-W_a-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-$ T-Q;

a, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently -C(O)-, -C(S)-, -T-, $-(C(R_e)(R_f))_h-$, an alkyl group, an aryl group, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

E at each occurrence is independently -T-, an alkyl group, an aryl group, $-(C(R_e)(R_f))_h-$, a heterocyclic ring, an arylheterocyclic ring, or $-(CH_2CH_2O)_q-$;

h is an integer form 1 to 10;

q is an integer from 1 to 5;

R_e and R_f are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, an alkylcycloalkyl, an alkylheterocyclic ring, a cycloalkylalkyl, a cycloalkylthio, a cycloalkenyl, an heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cyano an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfonyl, arylsulphonyloxy, a sulfonic ester, a urea, a phosphoryl, a nitro, W_h, -T-Q , or $-(C(R_e)(R_f))_k$-T-Q, or R_e and R_f taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group, an aryl group, an oxime or a bridged cycloalkyl group;

k is an integer from 1 to 3;

T at each occurrence is independently a covalent bond, a carbonyl, an oxygen, $-S(O)_o-$ or $-N(R_a)R_i-$;

o is an integer from 0 to 2;

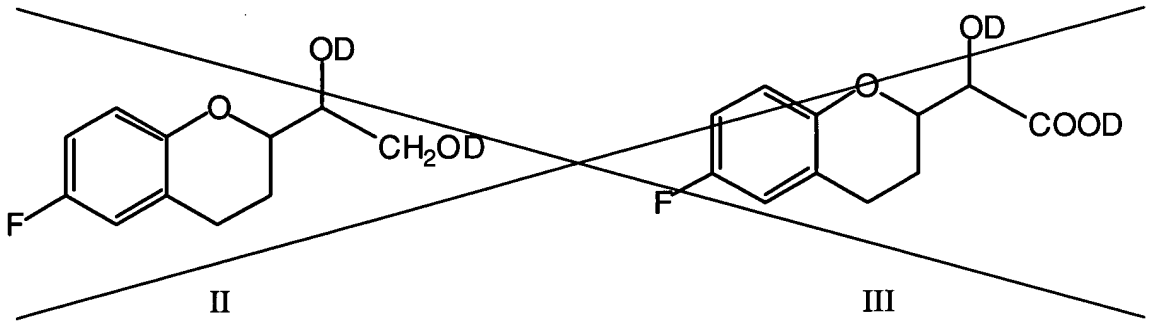
R_a is a lone pair of electrons, a hydrogen or an alkyl group;

R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an

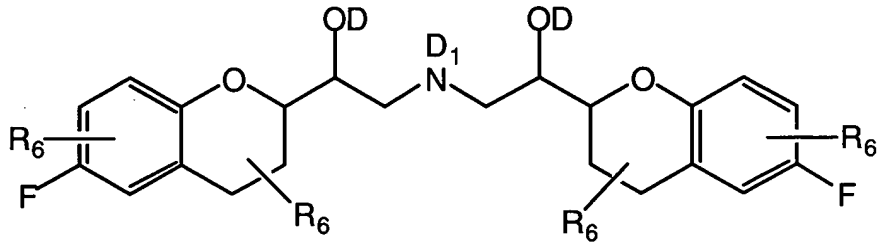
alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an alkylsulfonyloxy, an arylsulfinyl, an arylsulfonyl, arylsulphonyloxy, a sulfonamido, a carboxamido, a carboxylic ester, an aminoalkyl, an aminoaryl, $-CH_2-C(T-Q)(R_e)(R_f)$, a bond to an adjacent atom creating a double bond to that atom, $-(N_2O_2-)^-\bullet M^+$, wherein M^+ is an organic or inorganic cation;

with the proviso that the compound of Formula (I) must contain at least one nitrite, nitrate, thionitrite or thionitrate group;

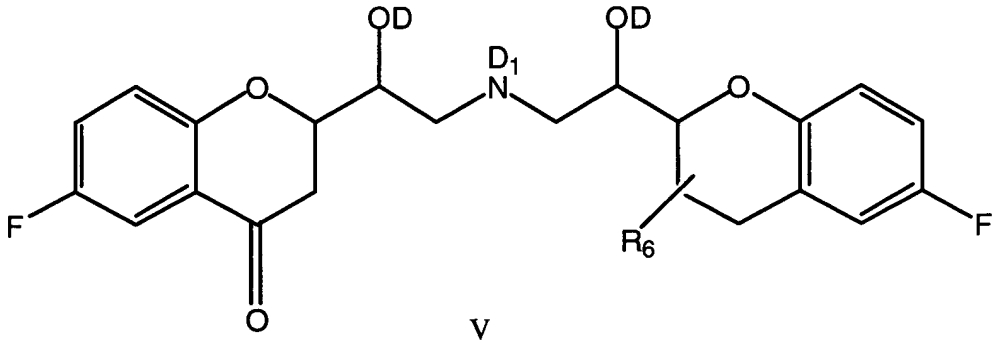
wherein the compounds of ~~Formula (II), Formula (III),~~ Formula (IV) and Formula (V) are:



II III



IV



V

wherein:

R_6 at each occurrence is independently a hydrogen, a hydroxy or -OD;

D and $D_1$is as defined herein; and

with the proviso that the compounds of ~~Formula (II), Formula (III),~~ Formula (IV) and Formula (V), must contain at least one nitrite, nitrate, thionitrite or thionitrate group.

75. (Original) The composition of claim 74, wherein the polymer is a synthetic polymer or a natural polymer selected from a polyolefin, a polyethylenimine, a polyethyleneimine derivative, a polyether, a polyanhydride, a polyhydroxybutyrate, a polyester, a polyamide, a polyurethane, a biopolymer, a starburst dendrimer, or a mixture thereof.

76. (Original) The composition of claim 74, further comprising at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, or at least one therapeutic agent or a mixture thereof.

77. (Original) The composition of claim 76, wherein the therapeutic agent is an antithrombogenic agent, a thrombolytic agent, a fibrinolytic agent, a vasospasm inhibitor, a potassium channel activator, a calcium channel blocker, an antihypertensive agent, an antimicrobial agent, an antibiotic, an antiplatelet agent, an antimitotic agent, an antiproliferative agent, a microtubule inhibitor, an antisecretory agent, a remodelling inhibitor, an antisense nucleotide, an anti-cancer chemotherapeutic agent, a steroid, a non-steroidal antiinflammatory agent, a selective COX-2 inhibitor, an immunosuppressive agent, a growth factor antagonist or antibody, a dopamine agonist, a radiotherapeutic agent, a heavy metal functioning as a radiopaque agent, a biologic agent, an angiotensin converting enzyme inhibitor, an angiotensin II receptor antagonist, a renin inhbitior, a free radical scavenger, an iron chelator, an antioxidant, a sex hormone, an antipolymerase, an antiviral agent, a photodynamic therapy agent, an antibody targeted therapy agent, a gene therapy agent, or a mixture thereof.

78. (Original) A method for direct delivery of nitric oxide to a targeted site in a patient in need thereof comprising administering the composition of claim 74 or 76 directly to the targeted site in the patient.

79. (Original) The method of claim 78, wherein the composition provides sustained delivery of nitric oxide to the targeted sited in the patient.

80. (Currently Amended) A medical device comprising the composition of claim 74 or 76, wherein the medical device is a balloon, a catheter tip, a stent, a catheter, a prosthetic heart valve, a synthetic vessel graft, an arteriovenous shunt, a heart valve, a suture, a vascular implant, a drug pump, a drug delivery catheter, plastic tubing, a dialysis bag, a lead, a pacemaker, an implantable pulse generator, an implantable cardiac defibrillator, a cardioverter defibrillator, a defibrillator, a spinal stimulator, a brain stimulator, a sacral nerve stimulator, a chemical sensor or a membrane surface.

81. (Original) The medical device of claim 79, wherein the composition coats all or a portion of the surface of the medical device.

82. (Original) The medical device of claim 80, wherein the composition forms all or part of the medical device.

83. (Cancelled)

84. (Currently Amended) A method for ~~the prevention of~~ treating platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device comprising incorporating at least one composition of claim 74 or claim 76 or a pharmaceutically acceptable salt thereof, into or on the medical device.

85. (Original) The method of claim 84, wherein the medical device is a balloon, a catheter tip, a stent, a catheter, a prosthetic heart valve, a synthetic vessel graft, an arteriovenous shunt, a heart valve, a suture, a vascular implant, a drug pump, a drug delivery catheter, plastic tubing, a dialysis bag, a lead, a pacemaker, an implantable pulse generator, an implantable cardiac defibrillator, a cardioverter defibrillator, a defibrillator, a spinal stimulator, a brain stimulator, a sacral nerve stimulator, a chemical sensor or a membrane surface.

86. (Original) The method of claim 84, wherein the blood is a blood product or a blood component.

87. (Currently Amended) A method for treating injured tissue in a patient in need thereof comprising administering at least one composition of claim 74 or 76 or a pharmaceutically acceptable salt thereof, to the site of the injured tissue in the patient, wherein the injured tissue is a blood vessel.

88. (Cancelled)

89. (Original) The method of claim 87, wherein the compound is administered to the site of the injured tissue via at least one of a suture, a vascular implant, a stent, a heart valve, a drug pump or a drug delivery catheter.

90. (Original) A kit comprising at least one compound of claim 3 and at least one compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, or a pharmaceutically acceptable salt thereof.

91. (Currently Amended) The kit of claim 90, further comprising at least one antioxidant and/or at least one angiotensin-converting enzyme inhibitor, beta-adrenergic blocker, cholesterol reducer, calcium channel blocker, angiotensin II receptor antagonist, endothelin antagonist, or renin inhibitor, ~~compound used to treat cardiovascular diseases~~, wherein the antioxidant is a small-molecule antioxidant, or a pharmaceutically acceptable salt thereof, or an antioxidant enzyme.

92. (Original) The kit of claim 90, wherein the compound of claim 3 and the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase are separate components in the kit or as a composition in the kit.

93-108. (Cancelled)